NIL -

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
JDH/2297PC		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB 00/02881	26/07/2000	22/07/1999
Applicant		
SMITH & NEPHEW plc		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. –

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 00/02881

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07C69/86

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	BRYAN GREENER: "Melt supramolecular assembly of oligomers with regularly spaced, alternating hydrogen bonding and hydrophobic sites " CHEMICAL COMMUNICATIONS., 1999, pages 2361-2362, XP002150429 ROYAL SOCIETY OF CHEMISTRY., GB ISSN: 1359-7345 the whole document	1-14

☐ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 October 2000	07/11/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Kinzinger, J

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INTERNATIONAL SEARCH REPORT

Int. Ional Application No
PCT/GB 00/02881

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07C69/86

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	BRYAN GREENER: "Melt supramolecular assembly of oligomers with regularly spaced, alternating hydrogen bonding and hydrophobic sites " CHEMICAL COMMUNICATIONS., 1999, pages 2361-2362, XP002150429 ROYAL SOCIETY OF CHEMISTRY., GB ISSN: 1359-7345 the whole document	1-14

☐ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 October 2000	07/11/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Kinzinger, J

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PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing: 01 February 2001 (01.02.01)	
International application No.: PCT/GB00/02881	Applicant's or agent's file reference: JDH/2297PC
International filing date: 26 July 2000 (26.07.00)	Priority date: 27 July 1999 (27.07.99)
Applicant: GREENER, Bryan	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International preliminary Examining Authority on:

20 November 2000 (20.11.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer:

J. Zahra

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

REC'D 08 JUN 2001
WIPO PCT

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
JDH/2297PC		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/02881	26/07/2000	27/07/1999
International Patent Classification (IPC) or national classification and IPC C07C69/86		
Applicant SMITH & NEPHEW plc		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
20/11/2000	06.06.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Slootweg, A Telephone No. +49 89 2399 8326

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02881

I. Basis f th report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-17 as originally filed

Claims, No.:

1-14 as originally filed

Drawings, sheets:

1/4-4/4 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application.

   ☒ claims Nos. 1-4,7-14.

because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

   ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-14 are so unclear that no meaningful opinion could be formed (*specify*):
   see separate sheet

   ☒ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the standard.

   ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

   Novelty (N) Yes: Claims

	No:	Claims	5, 6
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-14
Industrial applicability (IA)	Yes:	Claims	
	No:	Claims	1-14

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Due to the lack of clarity of the claims it is not at present possible to perform a full examination of the application.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive st p or industrial applicability; citations and explanations supporting such statem nt

2. Claim 5 is a claim towards compounds per sé. The fact that such a compound is capable of hydrogen bonding to form a supramolecular assembly is irrelevant when judging the patentability of the compounds. It is considered that a compound falling under this claim can also be a protein having side chains which can have hydrogen bonding-properties, which can then build supra-molecular assemblies. Proteins falling within the given are certainly known from the prior art (see also under point VIII below). Claims 5 and 6 are, therefore, considered to lack novelty (Art 33 (2) PCT).

Re Item VI

Certain documents cited

1. The document D1 (BRYAN GREENER: 'Melt supramolecular assembly of oligomers with regularly spaced, alternating hydrogen bonding and hydrophobic sites ' CHEMICAL COMMUNICATIONS., 1999, pages 2361-2362, ROYAL SOCIETY OF CHEMISTRY., GB ISSN: 1359-7345) could become relevant under Art. 33 (3) PCT if the priority were found not to be valid.

Re Item VIII

Certain observations on the international application

3. Claim 1 represents a problem to be solved, which requires an inventive activity by the skilled man. The supramolecular assembly could, for example, be a peptide composition, wherein peptide carries side-chains having carboxyl and/or hydroxy

groups, which have hydrogen-bonding properties. Peptides falling within the definition as given in claims 5 and 1 are certainly known from the prior art (although no documents were cited in the search report). Such peptides and assemblies thereof are not considered to be supported by the application. Claims 1-6 are not, therefore, considered to satisfy Art. 6 PCT.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
1 February 2001 (01.02.2001)

PCT

(10) International Publication Number
WO 01/07396 A1

(51) International Patent Classification[7]: C07C 69/86

(21) International Application Number: PCT/GB00/02881

(22) International Filing Date: 26 July 2000 (26.07.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
9917461.7 27 July 1999 (27.07.1999) GB

(71) Applicant *(for all designated States except US)*: **SMITH & NEPHEW PLC** [GB/GB]; Heron House, 15 Adam Street, London WC2N 6LA (GB).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: **GREENER, Bryan** [GB/GB]; 9 Beck Close, Elvington, York YO41 4BG (GB).

(74) Agent: **GROUP PATENTS & TRADE MARKS DEPARTMENT**; Smith & Nephew Group Research Centre, York Science Park, Heslington, York YO10 5DF (GB).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *With international search report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/07396 A1

(54) Title: HYDROGEN BONDED COMPOUNDS

(57) Abstract: A supramolecular assembly comprises a plurality of hydrogen bonded, aptly pharmacologically acceptable molecules. Each molecule contains, multiple site hydrogen bonding groups and at least a proportion of the molecules are bonded to other molecules at sites other than at terminal locations. Artefacts, which may be produced by drawing, extrusion or moulding include fibres, adhesives, medical devices such as fixation plates, screws or tissue anchors and biodegradable structural packaging materials.

HYDROGEN BONDED COMPOUNDS

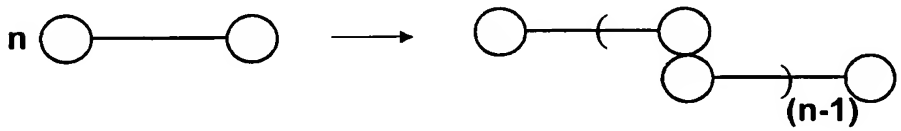
This invention relates to degradable polymer-like materials, in particular to such materials which are biodegradable, to precursors therefor and to artefacts made therefrom such as medical implant devices. More particularly the invention relates to polymer-like materials which can be formed into flexible constructs such as structural blocks, yarns and fibres.

In the conventional understanding of the term polymer, literally, many units, the component sub-units or precursors, eg. monomers or oligomers are bonded together *via* covalent linkages to form a high molecular weight material. Degradation of the polymer into lower molecular weight species occurs by scission of the covalent bonds binding the sub-units or by scission of a bond within one or more of the sub-units. For materials to biodegrade, the scission mechanism is usually a hydrolytic reaction. For a covalently bound polymer artefact to biodegrade completely, the hydrolysis of the polymer may take several years. Thus such polymers may have limited use in environments where constructs made from such polymers are required to have a temporary existence. Even in those cases where hydrolysis of the covalent bond, for example an anhydride linkage, takes place rapidly there has been no ability to control the precise nature of the degradation product. Thus, in some instances it may be desirable to degrade the polymer to lower molecular weight, non-toxic molecules, such as carbon dioxide and water, but in others it may be desired to form degradation products which are, themselves, beneficial, for example, exhibit a pharmaceutical effect.

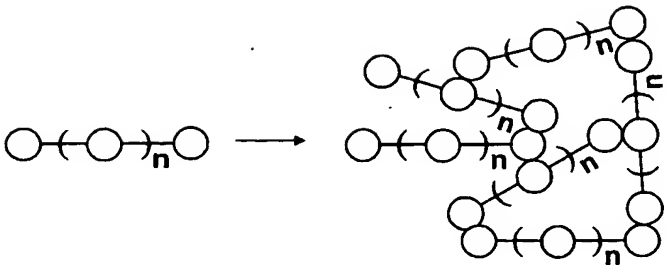
Thus, as an object, the present invention seeks to provide a class of materials which are capable of being formed into artefacts

and yet can be degraded in a predictable and controlled manner to form predictable fragments.

The materials of the present invention are characterised in that although they are polymer-like, the precursor residues are bonded to each other not by covalent bonds but by hydrogen bonds. Previously, this approach has been successfully applied to produce polymeric species by association of molecules with hydrogen bonding groups at their termini (for example, see R. P. Sijbesma, F. H. Beijer, L. Brunsveld, B. J. B. Folmer, J. H. K. K. Hirschberg, R. F. M. Lange, J. K. L. Lowe and E. W. Meijer, *Science*, **1997**, *278*, 1601 and references cited therein):



Such materials have been reported to be linear polymers, with each sub-unit associated to its neighbour at one site (which may be comprised of several hydrogen bonding groups). Because every chain is only as strong as its weakest link, researchers have focused on maximising the number of terminal hydrogen bonding groups. In a departure from this approach, we have produced molecules with multiple, regularly spaced hydrogen bonding sites and, in particular, at non-terminal sites, distinct from the prior art in that intermolecular interactions may occur at many sites and in a networked fashion:



The attachment of molecular components at many interactive sites affords less opportunity for dissociation than those hydrogen bonded molecules or 'assemblies' with only terminal interaction sites reported for prior art species.

In accordance with a first embodiment of the present invention there is provided a supramolecular assembly comprising a plurality of hydrogen bonded molecules, preferably pharmacologically acceptable molecules, each molecule contains multiple site hydrogen bonding groups and wherein at least a proportion of the molecules are bonded to other molecules at sites other than at terminal locations. Aptly the multiple site hydrogen bonding groups are regularly spaced.

In a preferred form of this embodiment the hydrogen bonding sites will be separated by hydrophobic moieties such as a moiety derived from an alkyl diacid

In accordance with a further embodiment of the invention there is provided a compound that is capable of being hydrogen bonded to form a supramolecular assembly and which has the general formula **(I)**:

$$\mathbf{A\text{-}X\text{-}(N\text{-}X)_n\text{-}A} \qquad \mathbf{(I)}$$

where:

A may be the same or different and is a moiety containing at least one hydrogen bond donor and/or acceptor site,

N may be the same or different and is a moiety containing at least one hydrogen bond donor and/or acceptor,

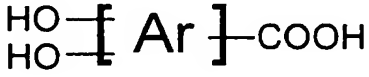
X may be the same or different and is a difunctional spacer linkage or unit

and **n** is an integer having a value of at least one.

In a further embodiment of the invention there is provided a biodegradable composition of matter comprising a super assembly of molecules each having the general formula (I) herein. More preferably, **A** and **N** will contain a plurality of hydrogen bond donor or acceptor sites, typically regularly spaced apart. The **A** moiety will contain at least four hydrogen bond donor or acceptor sites

The moieties **A** and **N**, containing the donor and/or acceptance sites or groups, may be known *per se*. Preferred moieties are those that contain hydroxyl and/or carboxyl groups.

Aptly, **A** is an aromatic moiety. preferably an aromatic moiety of the general formula **(II)**:

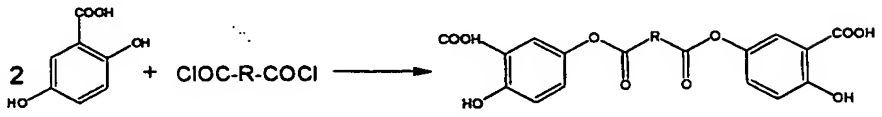


(II)

Where **Ar** is an unsubstituted or substituted aromatic nucleus e.g. phenyl or benzyl.

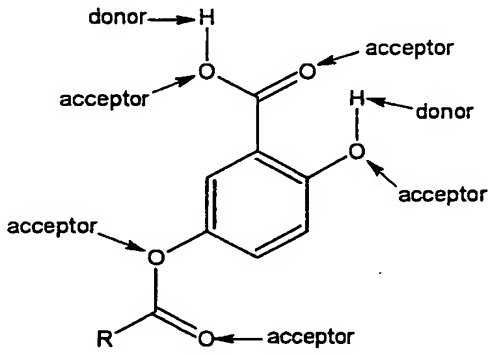
Preferred examples of compounds of Formula II are moieties which are capable of site-specific reactivity with the moiety **X**. Such preferred compounds include 2,5- and 2,3-dihydroxybenzoic acids

For example, when **X** is an alkyl diacid chloride, 2,5 dihydoxybenzoic acid will react according to the equation:



$R = (CH_2)_m$

The disposition of the terminal donor and acceptor sites in this compound may be represented thus:



N is a moiety containing at least one hydrogen bond acceptance or donation site, aptly two or more hydrogen bond donation or acceptance sites, and may preferably contain at least three donors and/or acceptors. Preferably **N** is a moiety which comprises both hydrogen bond donating and accepting sites regularly spaced,

The moiety **N** may be the same or different as the moiety **A**. Aptly, where **A** and **N** are different, **A** may be 2,5-dihydroxybenzoic acid and **N** may be 3,5-dihydroxybenzoic acid.

X is a difunctional linkage or residue and may be any moiety which does not have an adverse effect on the properties of the donor or acceptor groups. Suitably, **X** may comprise one or more

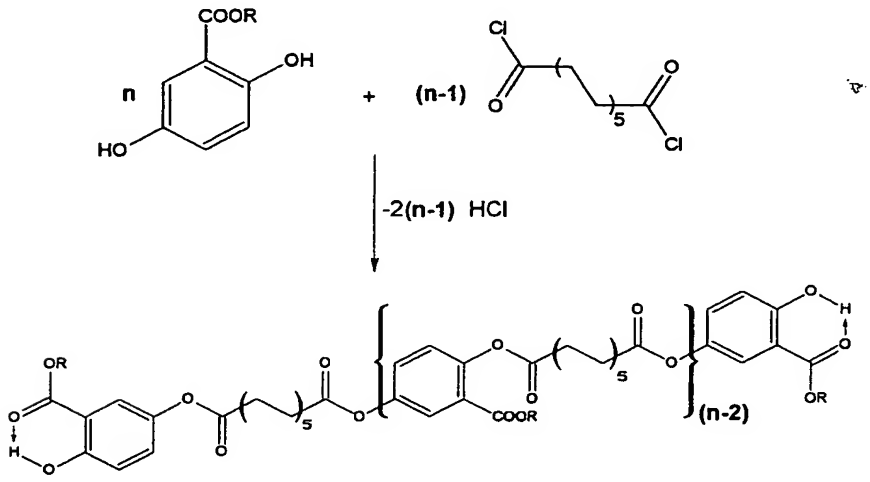
groups which exhibit hydrophobic properties. Aptly, **X** will be a residue which will impart flexibility to aggregates, mixtures or polymers derived from compounds of the invention.

X is preferably comprised, in part or in total, of an alkylene group $(CH_2)_m$ where $m \geq 2$ and more preferably, an alkyl diacid, or a functional derivative thereof, for example of the type,

$$HOOC\text{-}(CH_2)_m\text{-}COOH$$

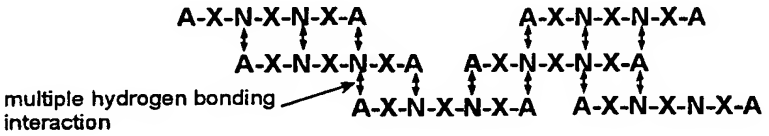
Aptly, the moiety **X** may be derived from long chain acids such as dodecanedioic-, decanedioic-, octanedioic- or hexanedioic acids or functional derivatives thereof such as dodecandioyl dichloride, suberoyl chloride or sebacoyl chloride.

Reactants comprising the precursors of the moieties **A** and **N** and **X** are reacted to form covalent linkages between the species. The methods employed to carry out this reaction may by those conventionally employed. For example, **A** or **N** may be connected to **X** *via* an ester linkage by reacting **A** or **N**, comprising of at least one hydroxyl function, with an acid halide of **X** as shown by the following reaction scheme:



The precursors of the supramolecular assemblies, being compounds and mixtures, as defined above, display aggregative properties in solution and/or in the molten state will henceforth be referred to as 'press-stud oligomers'. Aggregation of press-stud oligomers *via* the interaction of hydrogen bonding sites **A** and **N** allows the formation of supramolecular assemblies (in the form of fibres) when the press stud oligomer mass is melt extruded at elevated temperatures (>50 ^{0}C). Fibres so formed are self adherent and flexible immediately after extrusion. Aggregation can be probed by ^{13}C NMR spectroscopy and viscometric measurements against reference compounds lacking some/all hydrogen bonding functions.

The fibre forming properties of such aggregates, whilst not fully understood, are believed to be related to the abilility of the oligomers to align themselves under extrusion, as shown:



Press-stud oligomers are fibre-forming materials and may be composed of biocompatible and/or therapeutically active compounds (e.g. 2,5-dihydroxybenzoic acid) that are water soluble.

The press-stud oligomers of the present invention may be formed into supramolecular assemblies suitable for use as drug delivery vehicles and adhesives. The press-stud oligomers may be shaped into supramolecular assemblies suitable for medical device applications such as load-bearing fixation plates, screws or tissue anchors. In an alternative use the supramolecular assemblies of the

present invention may have uses outside the medical device field, for example as a biodegradable structural packaging material.

Accordingly, the present invention further provides an artefact formed from the biodegradable compositions of matter as described herein.

The invention will now be further described with reference to the accompanying drawings and the following examples, based on:

2,5-dihydroxybenzoic acid (**G**),
dodecanedioyl dichloride (**D**) and
methyl-2,5-dihydroxybenzoate (**MeG**)

all of which were supplied by Aldrich Chemical Co. Ltd and used as supplied.

In the structural formulae given abbreviations given in upper case text (e.g. $\mathbf{G_3D_4}$) refer to supramolecular assemblies whereas formulae expressed in lower case text (e.g. $\mathbf{g_3d_4}$) refer to the discrete press-stud oligomer form.

IR spectra were collected using a Mattson Galaxy 5020 FTIR spectrometer, samples prepared as cast films from THF for analysis. NMR spectra were collected using a JEOL 270 MHz NMR spectrometer.

Mass spectra were acquired using a Fisons Instruments Autospec Spectrometer. Viscometric measurements were performed using a Carrimed CSL500 constant stress rheometer, using a 4 cm diameter parallel plate and a 200 μm gap. Yields of >85% were recovered from all reactions.

Liquid Chromatography Conditions

Analyses were carri d out using a HP 1100 series chromatograph with a Jupiter C18 5μM 150 x 2mm column. Flow rate 0.2ml/min.

HP 1100 DAD 200 to 400nm detector. Samples were dissolved in methanol, injection volume 5 µl. Solvent gradient:

Time / min.	0.1% aqueous trifluoroacetic acid / %vol.	0.1% trifluoroacetic acid in acetonitrile / %vol.
0	50	50
5	50	50
20	10	90
40	10	90

Referring to the accompanying drawings:

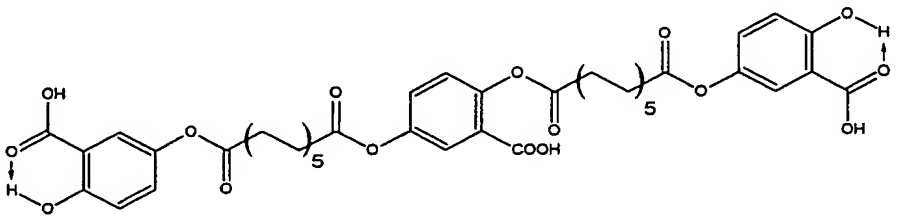
Figure 1. ^{1}H NMR (270 MHz, d_8-THF) spectra of oligomers, $\mathbf{G_nD_{n-1}}$ (top) and $\mathbf{MeG_nD_{n-1}}$ (bottom) in the aromatic region.

Figure 2. Infra-red absorbance spectra of $\mathbf{G_nD_{n-1}}$ (top) and $\mathbf{MeG_nD_{n-1}}$ (bottom) oligomers.

Figure 3. DAD HPLC of $\mathbf{G_3D_2}$ showing oligomeric components $\mathbf{g_2d_1}$, $\mathbf{g_3d_2}$, $\mathbf{g_4d_3}$ and $\mathbf{g_5d_4}$.

Figure 4. details the results of Variable temperature viscometric analysis of $\mathbf{G_nD_{n-1}}$ (top) and $\mathbf{MeG_nD_{n-1}}$ (bottom) oligomers.

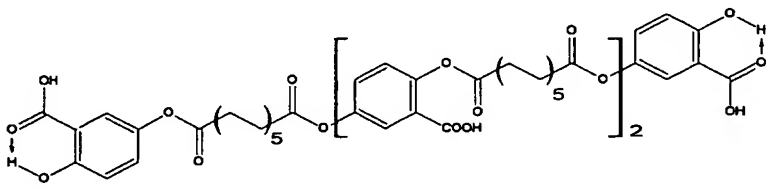
Example 1: Oligomers of the average structure G_3D_2:



A magnetically stirred melt of 2,5-dihydroxybenzoic acid (4.435 g, 29 mmol) **(G)**and dodecanedioyl dichloride (5.126 g, 19 mmol) **(D)**was heated from ambient temperature to 150 °C as rapidly as possible. Following 10 minutes stirring at this temperature, the viscous, transparent melt was poured from the vessel, solidifying to

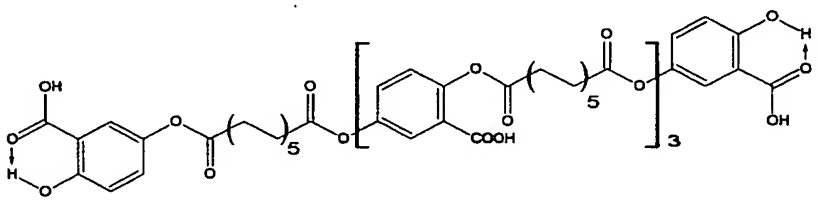
an opaque glass, and desiccated. IR / cm^{-1}: 1132, 1182, 1486, 1698, 1760, 2618, 2854, 2928, 3080. ^1H NMR (270 MHz; d_8-THF): δ11.04 (s (sharp), -OH); δ8.32 (s (broad), -COOH); 2,5-disubstituted **G**: δ7.72 (d, *J* 2.8, Ar-H); δ7.29 (dd, *J* 8.9, 2.8, Ar-H); δ7.08 (d, *J* 8.9, Ar-H); 5-substituted **G**: δ7.54 (d, *J* 2.8, Ar-H); δ7.18 (dd, *J* 8.9, 2.8, Ar-H); δ6.89 (d, *J* 8.9, Ar-H); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$). Electrospray MS -ve ion: 501.1 $\mathbf{g_2d_1}$ 849.2 $\mathbf{g_3d_2}$, 1197.3 $\mathbf{g_4d_3}$ ($M\text{-}H^+$).

Example 2: Oligomers of the average structure G_4D_3:



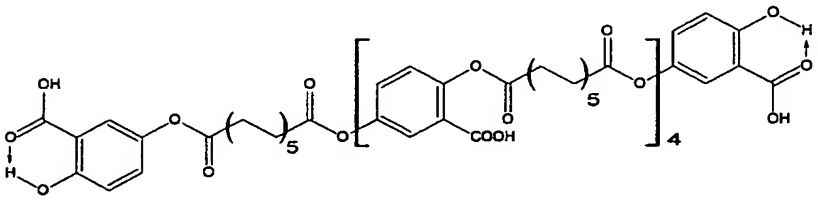
A magnetically stirred melt of 2,5-dihydroxybenzoic acid (4.115 g, 27 mmol) and dodecanedioyl dichloride (5.351 g, 20 mmol) was heated from ambient temperature to 150 °C as rapidly as possible. Following 10 minutes stirring at this temperature, the viscous, transparent melt was poured from the vessel, solidifying to an opaque glass, and desiccated. IR / cm^{-1}: 1132, 1182, 1486, 1698, 1760, 2618, 2854, 2928, 3080. ^1H NMR (270 MHz; d_8-THF): δ11.04 (s (sharp), -OH); δ8.32 (s (broad), -COOH); 2,5-disubstituted **G**: δ7.72 (d, *J* 2.8, Ar-H); δ7.29 (dd, *J* 8.9, 2.8, Ar-H); δ7.08 (d, *J* 8.9, Ar-H); 5-substituted **G**: δ7.54 (d, *J* 2.8, Ar-H); δ7.18 (dd, *J* 8.9, 2.8, Ar-H); δ6.89 (d, *J* 8.9, Ar-H); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$). Electrospray MS -ve ion: 501.1 $\mathbf{g_2d_1}$, 849.2 $\mathbf{g_3d_2}$, 1197.3 $\mathbf{g_4d_3}$, 1545.4 $\mathbf{g_5d_4}$, 1893.5 $\mathbf{g_6d_5}$ ($M\text{-}H^+$).

Example 3: Oligomers of the average structure G_5D_4:



A magnetically stirred melt of 2,5-dihydroxybenzoic acid (3.610 g, 23 mmol) **(G)**and dodecanedioyl dichloride (5.006 g, 19 mmol) **(D)**was heated from ambient temperature to 150 ^{0}C as rapidly as possible. Following 10 minutes stirring at this temperature, the viscous, transparent melt was poured from the vessel, solidifying to a semi-transparent glass, and desiccated. IR / cm^{-1}: 1132, 1182, 1486, 1698, 1760, 2618, 2854, 2928, 3080. ^{1}H NMR (270 MHz; d_8-THF): δ11.04 (s (sharp), -OH); δ8.32 (s (broad), -COOH); 2,5-disubstituted **G**: δ7.72 (d, *J* 2.8, Ar-H); δ7.29 (dd, *J* 8.9, 2.8, Ar-H); δ7.08 (d, *J* 8.9, Ar-H); 5-substituted **G**: δ7.54 (d, *J* 2.8, Ar-H); δ7.18 (dd, *J* 8.9, 2.8, Ar-H); δ6.89 (d, *J* 8.9, Ar-H); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$).

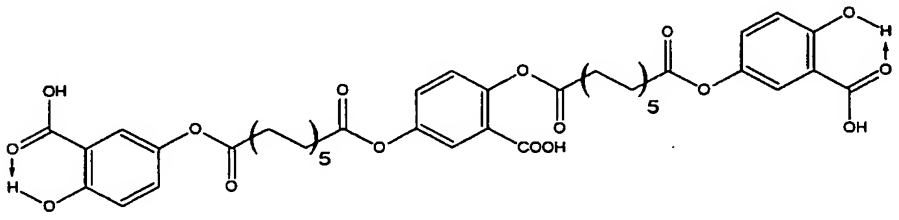
Example 4: Oligomers of the average structure G_6D_5:



A magnetically stirred melt of 2,5-dihydroxybenzoic acid (3.481 g, 23 mmol) **(G)**and dodecanedioyl dichloride (5.009 g, 19 mmol) **(D)** was heated from ambient temperature to 150 ^{0}C as rapidly as possible. Following 10 minutes stirring at this temperature, the viscous, transparent melt was poured from the vessel, solidifying to a semi-transparent glass, and desiccated. IR / cm^{-1}: 1132, 1182, 1486, 1698, 1760, 2618, 2854, 2928, 3080. ^{1}H NMR (270 MHz; d_8-

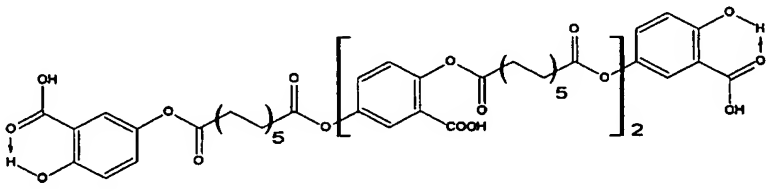
THF): δ11.04 (s (sharp), -OH); δ8.32 (s (broad), -COOH); 2,5-disubstituted **G**: δ7.72 (d, *J* 2.8, Ar-H); δ7.29 (dd, *J* 8.9, 2.8, Ar-H); δ7.08 (d, *J* 8.9, Ar-H); 5-substituted **G**: δ7.54 (d, *J* 2.8, Ar-H); δ7.18 (dd, *J* 8.9, 2.8, Ar-H); δ6.89 (d, *J* 8.9, Ar-H); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$).

Example 5: Oligomer of the structure g_3d_2:



The oligomer of average structure $\mathbf{G_3D_2}$ (example 1) was separated by preparative-scale LC into its constituent oligomeric components, resulting in the isolation of $\mathbf{g_3d_2}$. IR / cm^{-1}: 1132, 1182, 1486, 1698, 1760, 2618, 2854, 2928, 3080. ^{1}H NMR (270 MHz; d_8-THF): δ11.04 (s (sharp), -OH); δ8.32 (s (broad), -COOH); 2,5-disubstituted **G**: δ7.72 (d, *J* 2.8, Ar-H); δ7.29 (dd, *J* 8.9, 2.8, Ar-H); δ7.08 (d, *J* 8.9, Ar-H); 5-substituted **G**: δ7.54 (d, *J* 2.8, Ar-H); δ7.18 (dd, *J* 8.9, 2.8, Ar-H); δ6.89 (d, *J* 8.9, Ar-H); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$). Electrospray MS -ve ion: 849.2 ($M\text{-}H^+$).

Example 6: Oligomer of the structure g_4d_3:



The oligomer of average structure $\mathbf{G_3D_2}$ (example 1) was separated by preparative-scale LC into its constituent oligomeric components, resulting in the isolation of $\mathbf{g_4d_3}$. IR / cm^{-1}: 1132, 1182, 1486, 1698,

1760, 2618, 2854, 2928, 3080. ^{1}H NMR (270 MHz; d_8-THF): δ11.04 (s (sharp), -OH); δ8.32 (s (broad), -COOH); 2,5-disubstituted **G**: δ7.72 (d, *J* 2.8, Ar-H); δ7.29 (dd, *J* 8.9, 2.8, Ar-H); δ7.08 (d, *J* 8.9, Ar-H); 5-substituted **G**: δ7.54 (d, *J* 2.8, Ar-H); δ7.18 (dd, *J* 8.9, 2.8, Ar-H); δ6.89 (d, *J* 8.9, Ar-H); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$). Electrospray MS -ve ion: 1197.3 ($M\text{-}H^+$).

Example 7: Oligomer of the average structure G_3D_3

A magnetically stirred melt of 2,5-dihydroxybenzoic acid (7.518 g, 49 mmol) and dodecanedioyl chloride (13.034 g, 49 mmol) was heated to 150 °C. Following 10 minutes of heating at this temperature, the transparent viscous melt was cooled to room temperature and desiccated.

Mechanical Properties

The mechanical properties of some of the supramolecular assemblies of the present invention are given below.

Aluminium studs were provided with a raised circular portion 5mm in diameter. A melt of the oligomers listed in Table 1 were coated onto the raised circular portions and the coated circular portions two studs were brought and held together under hand pressure until the melt had cooled and solidified. For comparative purposes a pair of aluminium studs were joined together with a conventional cyanoacrylate adhesive in the same manner as the supra molecular assemblies of the invention

Each stud was held in the jaws of a Nene MC 30000 tensile testing machine and testing was carried out a speed of 5mm min^{-1}.

Table 1

Example	Oligomer	Load to break / N	Breaking strength / MPa
	G_2D_1	50	1.8
1	G_3D_2	413	15.1
2	G_4D_3	222	8.1
3	G_5D_4	105	3.8
4	G_6D_5	202	7.4
	Cyanoacrylate	193	7.1

For physical comparison with examples 1-4, equivalent oligomers were prepared using methyl-2,5-dihydroxybenzoate (**MeG**) in place of 2,5-dihydroxybenzoic acid:

COMPARATIVE EXAMPLES

(i) - Oligomers of average structure MeG_3D_2

A magnetically stirred melt of methyl-2,5-dihydroxybenzoate (2.461 g, 15 mmol) and dodecanedioyl dichloride (2.607 g, 10 mmol) was heated from ambient temperature to 150 °C as rapidly as possible. Following 10 minutes stirring at this temperature, the viscous, transparent melt was poured from the vessel, solidifying to an opaque glass, and desiccated. IR / cm^{-1}: 1129, 1212, 1486, 1682, 1731, 1761, 2854, 2928. ^1H NMR (270 MHz; d_8-THF): δ10.60 (2H, s (sharp), -OH); 2,5-disubstituted **MeG**: δ7.69 (d, *J* 3.0, Ar-H); δ7.31 (dd, *J* 8.7, 2.8, Ar-H); δ7.11 (d, *J* 8.7, Ar-H); δ3.78 (s, CH_3); 5-substituted **MeG**: δ7.52 (d, *J* 3.0, Ar-H); δ7.21 (dd, *J* 8.7, 3.0, Ar-H); δ6.93 (d, *J* 8.7, Ar-H); δ3.91 (s, CH_3); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$).

(ii) - Oligomers of average structure MeG_4D_3

A magnetically stirred melt of methyl-2,5-dihydroxybenzoate (2.426 g, 14 mmol) and dodecanedioyl dichloride (2.892 g, 11 mmol) was heated from ambient temperature to 150 °C as rapidly as possible. Following 10 minutes stirring at this temperature, the viscous, transparent melt was poured from the vessel, solidifying to an

opaque glass, and desiccated. IR / cm^{-1}: 1129, 1212, 1486, 1682, 1731, 1761, 2854, 2928. ^1H NMR (270 MHz; d_8-THF): δ10.60 (2H, s (sharp), -OH); 2,5-disubstituted **MeG**: δ7.69 (d, *J* 3.0, Ar-H); δ7.31 (dd, *J* 8.7, 2.8, Ar-H); δ7.11 (d, *J* 8.7, Ar-H); δ3.78 (s, CH_3); 5-substituted **MeG**: δ7.52 (d, *J* 3.0, Ar-H); δ7.21 (dd, *J* 8.7, 3.0, Ar-H); δ6.93 (d, *J* 8.7, Ar-H); δ3.91 (s, CH_3); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$).

(iii) - Oligomers of average structure MeG_5D_4

A magnetically stirred melt of methyl-2,5-dihydroxybenzoate (3.934 g, 23 mmol) and dodecanedioyl dichloride (5.013 g, 19 mmol) was heated from ambient temperature to 150 ^0C as rapidly as possible. Following 10 minutes stirring at this temperature, the viscous, transparent melt was poured from the vessel, solidifying to a semi-transparent glass, and desiccated. IR / cm^{-1}: 1129, 1212, 1486, 1682, 1731, 1761, 2854, 2928. ^1H NMR (270 MHz; d_8-THF): δ10.60 (2H, s (sharp), -OH); 2,5-disubstituted **MeG**: δ7.69 (d, *J* 3.0, Ar-H); δ7.31 (dd, *J* 8.7, 2.8, Ar-H); δ7.11 (d, *J* 8.7, Ar-H); δ3.78 (s, CH_3); 5-substituted **MeG**: δ7.52 (d, *J* 3.0, Ar-H); δ7.21 (dd, *J* 8.7, 3.0, Ar-H); δ6.93 (d, *J* 8.7, Ar-H); δ3.91 (s, CH_3); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$).

(iv) - Oligomers of average structure MeG_6D_5

A magnetically stirred melt of methyl-2,5-dihydroxybenzoate (3.778 g, 23 mmol) and dodecanedioyl dichloride (5.016 g, 19 mmol) was heated from ambient temperature to 150 ^0C as rapidly as possible. Following 10 minutes stirring at this temperature, the viscous, transparent melt was poured from the vessel, solidifying to a semi-transparent glass, and desiccated. IR / cm^{-1}: 1129, 1212, 1486, 1682, 1731, 1761, 2854, 2928. ^1H NMR (270 MHz; d_8-THF): δ10.60 (2H, s (sharp), -OH); 2,5-disubstituted **MeG**: δ7.69 (d, *J* 3.0, Ar-H);

δ7.31 (dd, *J* 8.7, 2.8, Ar-H); δ7.11 (d, *J* 8.7, Ar-H); δ3.78 (s, CH_3); 5-substituted **MeG**: δ7.52 (d, *J* 3.0, Ar-H); δ7.21 (dd, *J* 8.7, 3.0, Ar-H); δ6.93 (d, *J* 8.7, Ar-H); δ3.91 (s, CH_3); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$).

The MeG-oligomers so produced differed from the examples of the invention in that the potential for intermolecular acid hydrogen bonding had been removed.

Structural and oligomeric homology between the **G**-based and **MeG**-based oligomers was confirmed by ^1H NMR spectroscopy, as shown in Figure 1. The presence of acidic hydrogen bonding functionality in the **G**-based oligomers and the absence of such functionality in **MeG**-based oligomers manifested itself when the IR spectra of the two series were compiled and compared, as seen in Figure 2. The absorbance band-broadening observed in the carbonyl region (ca. 1700 cm^{-1}) for **G**-based oligomers is indicative of several hydrogen bonding environments, in comparison with relatively sharp absorbances in corresponding **MeG**-based oligomers.

The oligomeric distribution for examples of average structure was determined by liquid chromatography with a UV-vis diode array detector. The results shown in Figure 3 illustrate the distribution of oligomers in the Supramolecular Assembly described in Example 1. The proposed physical effect of multiple-site intermolecular hydrogen bonding interactions was confirmed by variable temperature viscometric study of **G**-based and **MeG**-based oligomers, as shown in Figure 4. The viscosities for **G**-based oligomers were consistently greater than those observed for **MeG**-based oligomers by *ca.* 40-fold. It can also be seen that, in general, viscosities increased, throughout the temperature range observed,

as the average oligomeric length increased. Viscosities increased with a greater rate towards solidification as the average oligomeric length increased. These observations are in accordance with an increasing number of intermolecular hydrogen bonding interactions and entanglements.

All $\mathbf{G_nD_{n-1}}$ oligomers formed fibres from the molten state that became brittle after several minutes at room temperature; $\mathbf{MeG_nD_{n-1}}$ oligomers were non-fibre-forming. All $\mathbf{G_nD_{n-1}}$ and $\mathbf{MeG_nD_{n-1}}$ oligomers cooled to semi-transparent glasses.

CLAIMS

1. A supramolecular assembly comprising a plurality of hydrogen bonded molecules, each molecule contains regularly spaced, multiple site hydrogen bonding groups and wherein at least a proportion of the molecules are bonded to other molecules at sites other than at terminal locations

2 An assembly as claimed in claim 1 wherein the hydrogen bonded molecules are pharmacologically acceptable

3. An assembly as claimed in claim 1 or claim 2 wherein the hydrogen bonding sites are separated by hydrophobic moieties

4. An assembly as claimed in any one of claims 1 to 3 wherein the hydrophobic moiety is derived from an alkyl diacid or functional derivative thereof

5. A compound that is capable of being hydrogen bonded to form a supramolecular assembly having the general formula **(I)**:

$$A\text{-}X\text{-}(N\text{-}X)_n\text{-}A \qquad (I)$$

where:

A may be the same or different and is a moiety containing at least one hydrogen bond donor and/or acceptor sites,

N may be the same or different and is a moiety containing at least one hydrogen bond donor and/or acceptor,

X may be the same or different and is a difunctional spacer linkage or unit

and **n** is an integer having a value of at least one.

6. A compound as claimed in claim 5 wherein the moieties **A** and **N**, contain hydroxyl or carboxyl groups

7. A compound as claimed in claim 5 or claim 6 wherein **A** is an aromatic moiety of the general formula **(II)**:

(II)

Where **Ar** is an unsubstituted or substituted aromatic nucleus.

8. A compound as claimed in any of claims to 7 wherein **Ar** is phenyl or benzyl

9. A compound as claimed in any of claims 5 to 8 wherein the compound of Formula (II) is 2,5- dihydroxybenzoic acid or 2,3-dihydroxybenzoic acid

10. A compound as claimed in any of claims 5 to 9 wherein **N** is a moiety containing at least three hydrogen bond acceptance or donation sites.

11. A compound as claimed in any of claims 5 to 10 wherein **X** is an alkyl diacid of the general formula:

$HOOC-(CH_2)_m-COOH$

Wherein m is an integer having a value of at least 2, or a functional derivative thereof

12. A compound as claimed in Claim 11 wherein **X** is derived

from dodecanedioic-, decanedioic-, octanedioic- or hexanedioic acids or an acid chloride thereof

13. An assembly comprising the aggregation of compounds of the general formula (I) as defined in claim 5

14. An artefact manufactured from an assembly as claimed in any one of claims 1 to 4 or from a compound as claimed in any one of claims 5 to 13

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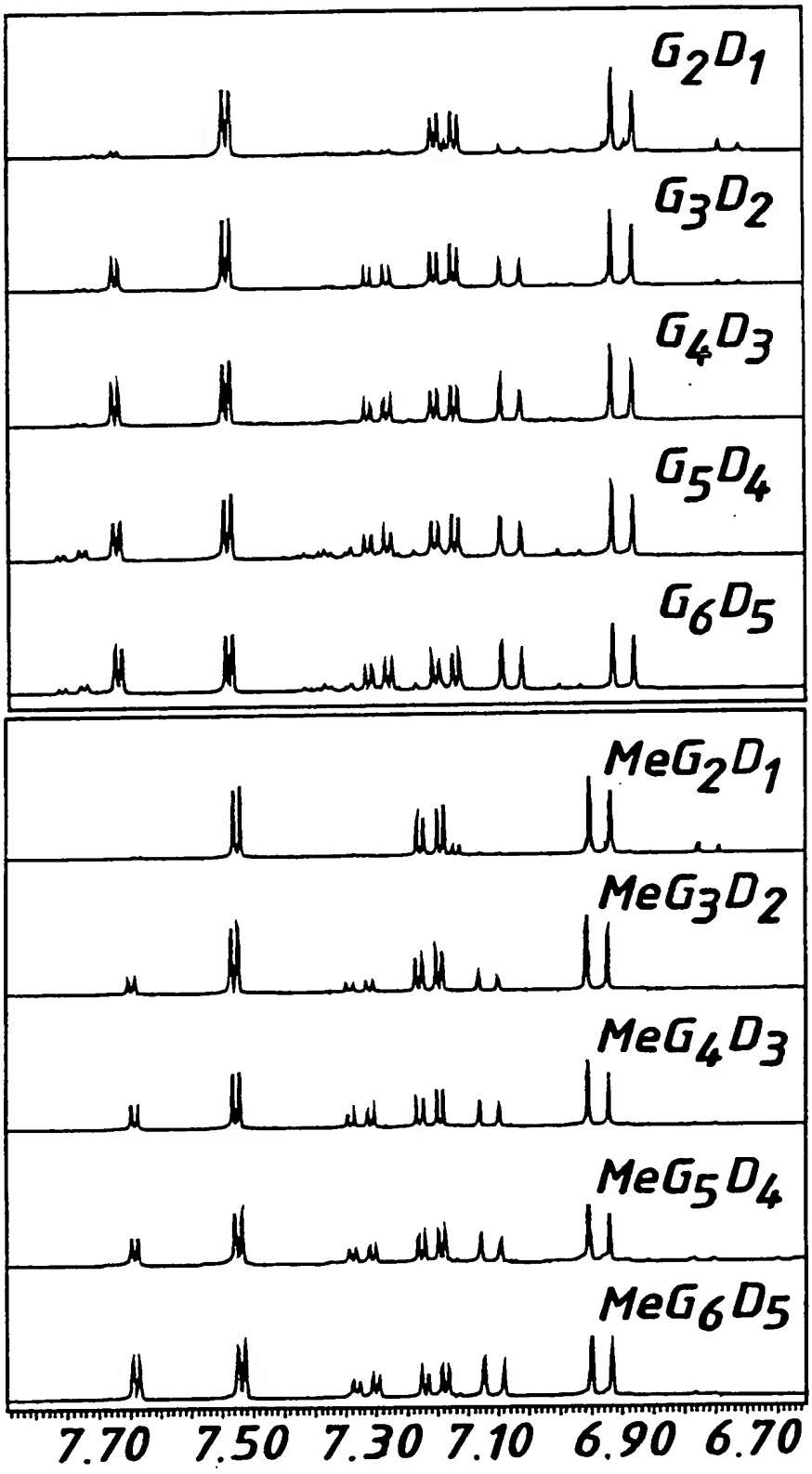
FIG. 1.


G_2D_1
G_3D_2
G_4D_3
G_5D_4
G_6D_5
MeG_2D_1
MeG_3D_2
MeG_4D_3
MeG_5D_4
MeG_6D_5
7.70 7.50 7.30 7.10 6.90 6.70
(ppm)

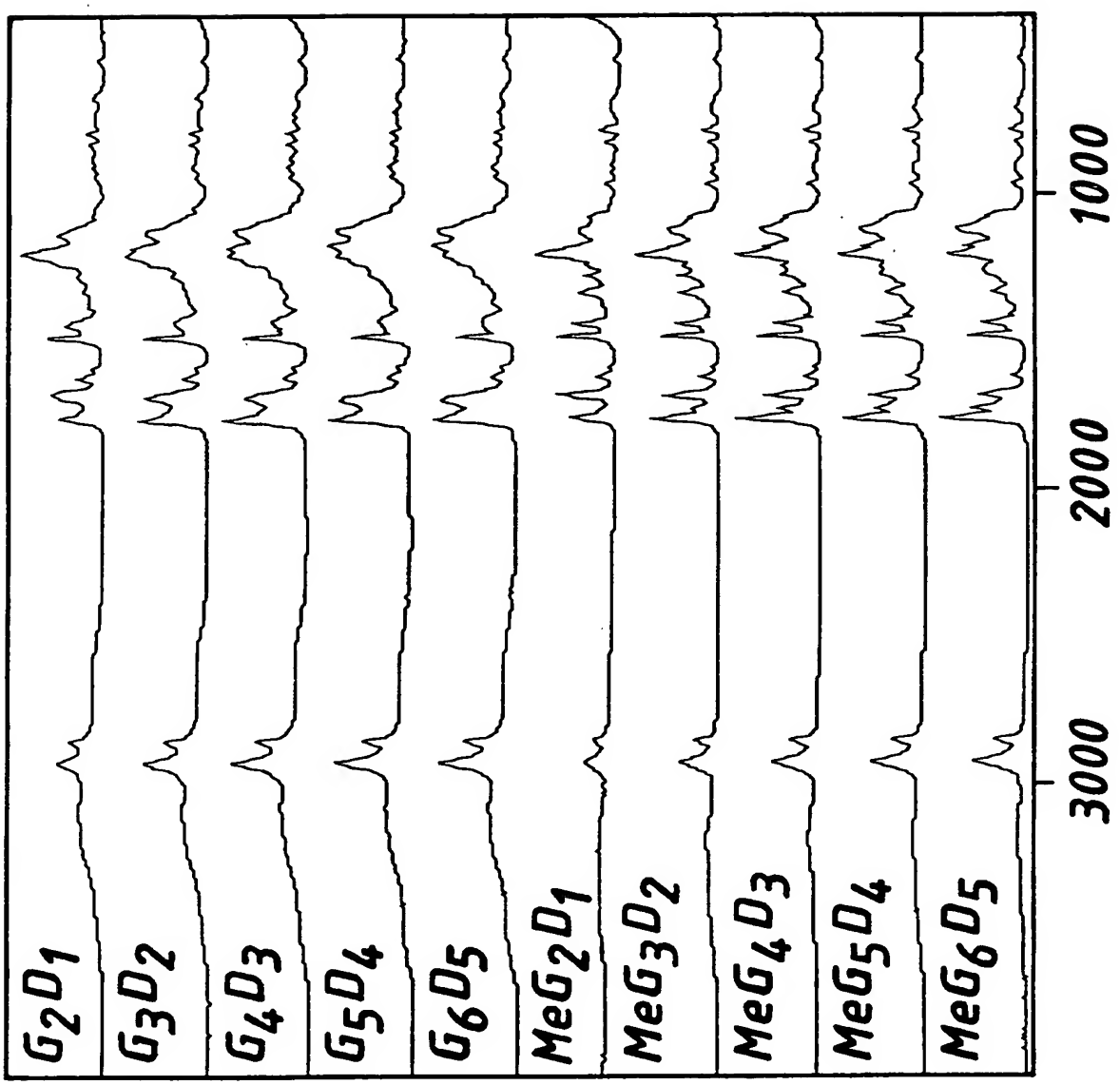

G_2D_1
G_3D_2
G_4D_3
G_5D_4
G_6D_5
MeG_2D_1
MeG_3D_2
MeG_4D_3
MeG_5D_4
MeG_6D_5
3000
2000
1000

FIG.2.

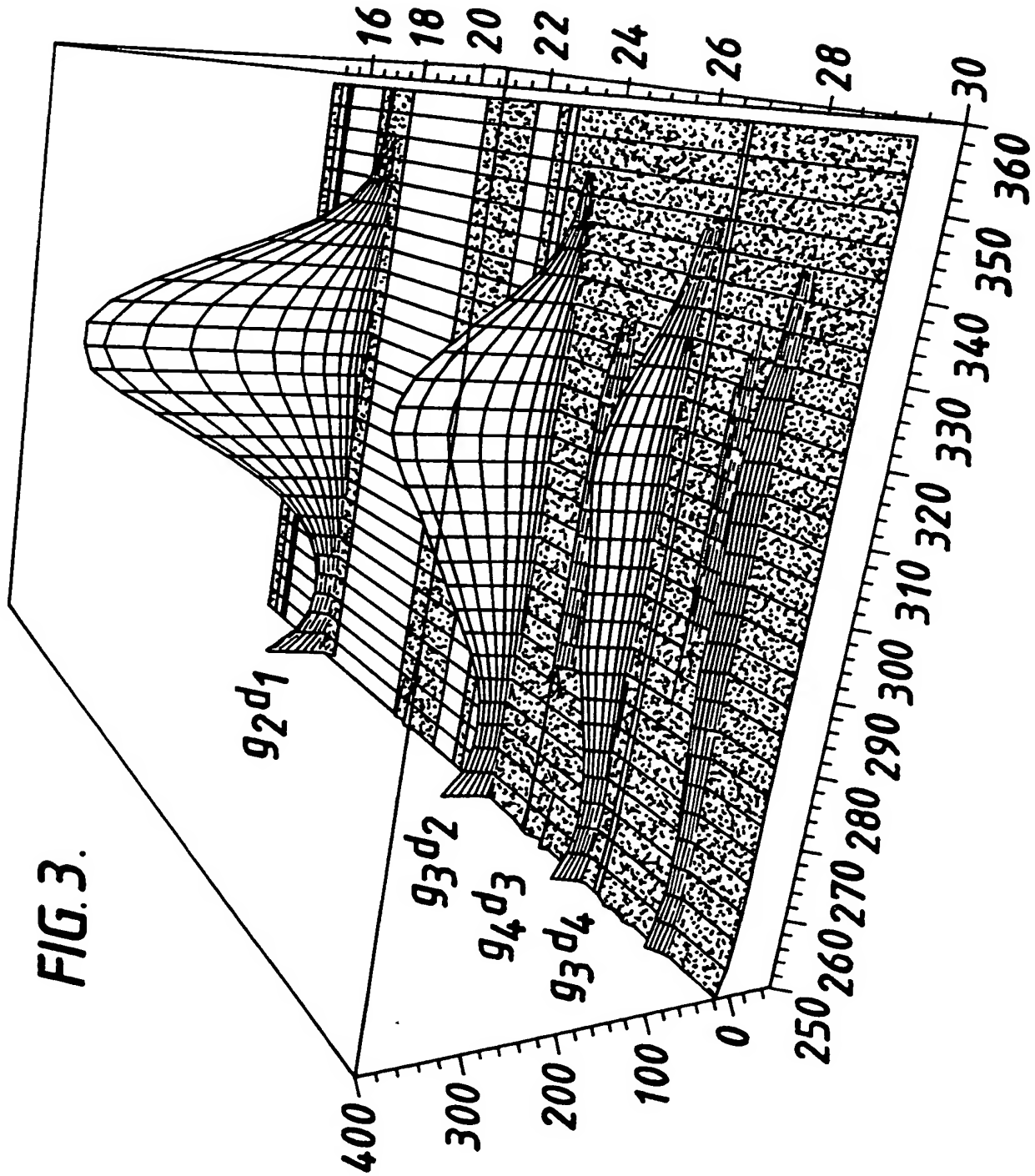

16
18
20
22
24
26
28
30
360
350
340
330
320
310
300
290
280
270
260
250
0
100
200
300
400
g_2d_1
g_3d_2
g_4d_3
g_3d_4

FIG.3.

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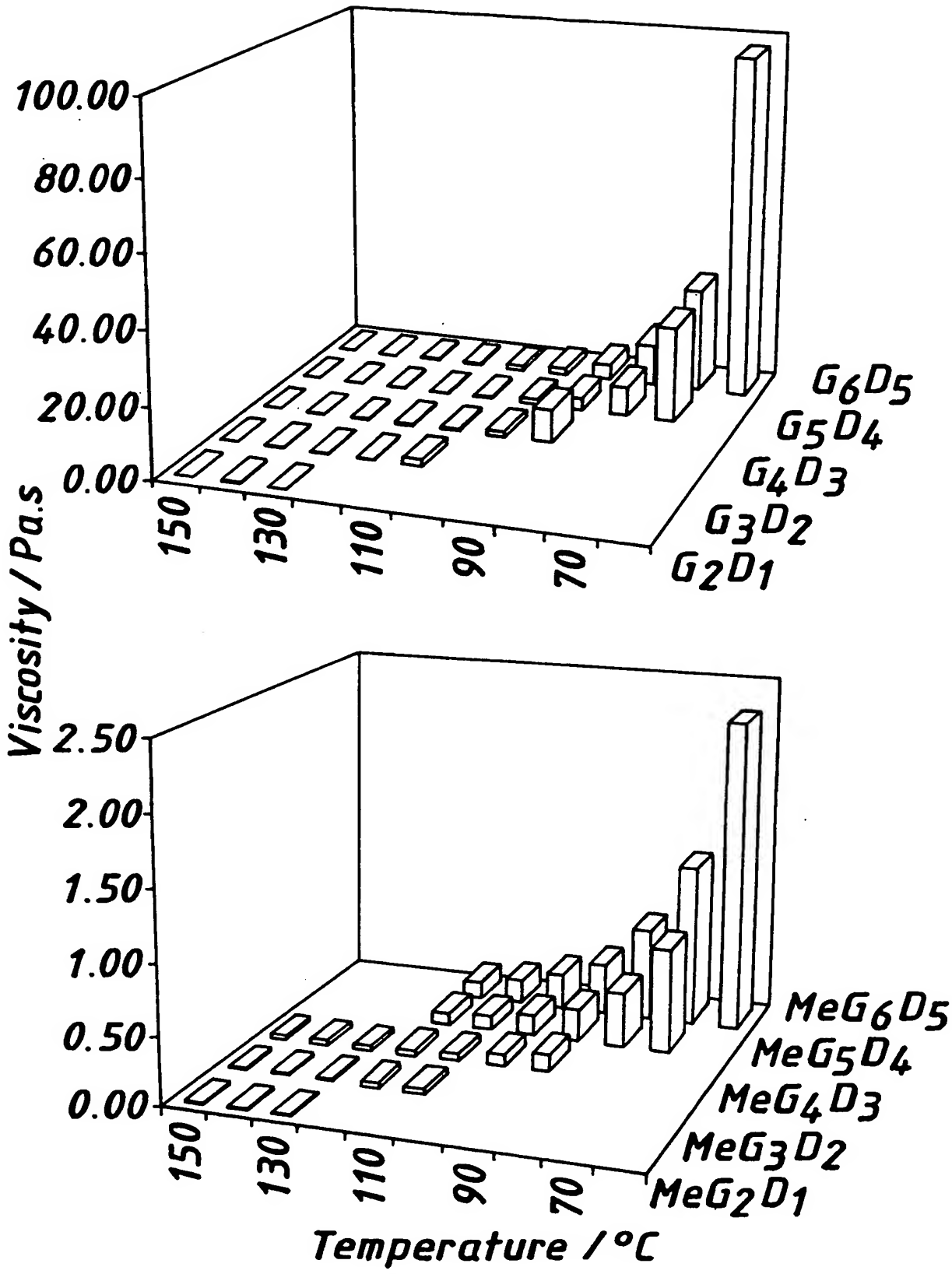
FIG. 4.


100.00
80.00
60.00
40.00
20.00
0.00
150
130
110
90
70
G6D5
G5D4
G4D3
G3D2
G2D1
2.50
2.00
1.50
1.00
0.50
0.00
MeG6D5
MeG5D4
MeG4D3
MeG3D2
MeG2D1
Viscosity / Pa.s
Temperature / °C

INTERNATIONAL SEARCH REPORT

Int. Ional Application No
PCT/GB 00/02881

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07C69/86

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	BRYAN GREENER: "Melt supramolecular assembly of oligomers with regularly spaced, alternating hydrogen bonding and hydrophobic sites " CHEMICAL COMMUNICATIONS., 1999, pages 2361-2362, XP002150429 ROYAL SOCIETY OF CHEMISTRY., GB ISSN: 1359-7345 the whole document	1-14

☐ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

* Special categories of cited documents :

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 October 2000	07/11/2000

Name and mailing address of the ISA	Authorized officer
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